IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Griffiths, *et al.*	Examiner:	Graser, Jennifer E.
Serial No.:	10/521,103	Art Unit:	1645
		Confirm. No.	5430
Filed:	February 14, 2005	Docket No.:	N079 1150 US (formerly VA/H-32534A)
For:	**HSP70 FROM ARTHROBACTER**		

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

DECLARATION UNDER 37 CFR §1.132

I, Nathalie Simard, do hereby declare and say as follows:

1. I have reviewed and am familiar with the contents of the above-referenced patent application. I have reviewed the Office Action mailed on February 7, 2008 and am familiar with the contents thereof.

2. I received my D.E.C. in Chemistry-Biology from the College of Lévis-Lauzon, Lauzon, Québec, Canada in 1989. I received my M.Sc. in Molecular Biology from the University of New Brunswick, New Brunswick, Canada in 2000.

I have over fourteen years experience in vaccine research focusing on biotechnology derived vaccines. I joined Novartis in 1999, and successively held the positions of Scientist and Senior Scientist. Prior to joining Novartis, I worked as a Laboratory Research Assistant, 1997-1998, New Brunswick Research and Productivity Council and previously as a Biochemistry Technologist, 1989-1993. I have been a recipient of a fellowship from the University of New Brunswick, New Brunswick Canada, in 1995-1996 and 1996-1997. Since 2003, I have been granted 2 United States patents, 2 European patents; and have 3 published international (PCT) patent applications (World Intellectual Property Organization international publications). I am the author of nearly 13 manuscripts, book chapters and

abstracts relating to my area of research. See attached Exhibit I, List of Publications of Ms. Nathalie Simard.

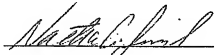
I have been with Novartis Animal Health, Canada, Inc. ("Novartis") since 1999. As Sr, Scientist of vaccine research, I am responsible for the oversight of developing novel DNA and bacterial recombinant vaccine against fish pathogens, the evaluation of new vaccine delivery systems and technology platforms, as well as the molecular engineering of biotechnology derived vaccines.

3. Since 1999, I have directed the molecular vaccine research, focusing on design and efficacy improvement through adjuvanting at Novartis. I am very familiar with the recent research discussed below, confirming and extending the observations disclosed in the present application.

4. The information provided in the present application represents the discovery of a surprising improvement in the relative percent survival in fish vaccinated with Hsp70-adjuvanted vaccines. In this regard, see attached Exhibit II, which demonstrates in Trial 1 that the pET30 Hsp-VP2 fusion provided the lowest cumulative percent mortality after an IPNV challenge compared to any of the other vaccines which are not Hsp-adjuvanted. In trial 2, the pET30 Hsp-VP2 again provided the lowest cumulative percent mortality. These two examples further demonstrate the improved level of survival in fish fry vaccinated with Hsp70-adjuvanted vaccines compared to all those which have used the antigen alone.

5. The invention also provides the benefit that injection of *Arthrobacter* hsp70 nucleic acid or protein into fish does not result in disfiguring swellings or nodules at the injection site compared to conventional *Mycobacterium* adjuvanted vaccines. *Arthrobacter* Hsp70 protein is not only effective in adjuvanting vaccines comprising other antigens, but it also has immunogenic activity in its own right. *Arthrobacter* Hsp70 can provide the active principle for a vaccine to prevent or treat a variety of diseases caused by fish pathogens.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Nathalie Simard, M.Sc..

28/07/2008

Date

Exhibit I
(List of Publications of Ms. Nathalie Simard)

Publications

- **Salonius, K., Simard, N., Harland, R., and Ulmer, J.B. 2007. The road to licensure of a DNA vaccine. Current Opinion in Investigational Drugs, 8(8):635-41.**

- **Ritchie, R.J., Cook, M., Melville, K., Simard, N., Cusack, R., and Griffiths, S. 2001. Identification of infectious salmon anaemia virus in Atlantic salmon from Nova Scotia (Canada): evidence for functional strain differences. Diseases of Aquatic Organisms, 44(3):171-8.**

- **Simard, N.C. 2000. Development of a DNA vaccine against *Renibacterium salmoninarum* in Atlantic salmon (*Salmo salar*). M.Sc. Thesis. University of New Brunswick, New Brunswick, Canada, 89 pp.**

Oral Presentations

Invited Key Note Speaker:

- **Simard, N.C. 2008. Genomics & Proteomics in Vaccine Development. NAH Marketing Summit – Key Account Meeting. Montreal, Que, Canada.**

- **Simard, N.C. 2006. Design of Vaccines for Fish: New Technologies for the Future. Primera Conferencia De Agua Dulce, Encuentro Annual Sketting.**

- **Simard, N.C., Lyngoy, C., Funk., V., Traxler, G., LaPatra, S., and Salonius, K. 2006. Research to market: meeting safety and efficacy requirements for a DNA vaccine used in Atlantic salmon. 4th International Veterinary Vaccines and Diagnostics Conference, June 25-29, Oslo, Norway.**

- **Simard, N.C., 2003. DNA Vaccination Against IHNV: Overview & Current Research. Novartis Animal Health. Cambpell River, BC, Canada.**

Oral Presentations:

- **Simard, N.C. 2007. Energizing the Aqua R&D Culture. Novartis Animal Health , First Global Research & Development Conference. Centre des Congrès, Paris, France.**

- **Simard, N., and Moores, D. 2006. DNA vaccines and Environmental Safety. 31th Eastern Fish Health Workshop. Mt. Pleasant, South Carolina, USA.**

Posters:

- **Salonius, K., Kibenge, F., Falk, K., Ritchie, R., Elliot, J., Pallapotu, M., Riveroll, A., and Simard, N. 2008. Mitigation of Infectious Salmon Anemia by vaccination and genetic selection. Poster. American Fisheries Scociety, Fish Health Section, Annual Meeting, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada.**

- **Roy, M., LaFlamme, M., Salonius, K., Simard, N.C., Robichaud-Hache, M., Robichaud, G.A., and Gagné, N. 2008. Development of a novel recombinant vaccine models against Infectious Salmon Anemia Virus (ISAV). American Fisheries Scociety, Fish Health Section, Annual Meeting, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada.**

- **Simard, N.C., and Horne, M.T. 2005. Evaluation of the systemic distribution and clearance rate of a plasmid DNA vaccine in Atlantic salmon (*Salmo salar L.*). European Association of Fish Pathologist – 12th International Conference, Copenhagen, Denmark.**

Abstracts

- **Salonius, K., Pallapothu, M., Simard, N., Phillips, L., Hickey, S., Kibenge, M., and Kibenge, F. 2008. Efficacy of ISA Vaccines derived from conventional, process refined, and recombinant DNA technologies. American Fisheries Scociety, Fish Health Section, Annual Meeting, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada.**

Exhibit 2

(Trial 1 & Trial 2)

Trial 1

Fish were vaccinated with IPNV at a body weight of 0.33g with the vaccine diluted to a fixed total protein content of 1.98 mg/ml. Fish were vaccinated by 1 minute immersion. Triplicate groups of 55 fish at body weight 0.490g were challenged with IPNV at 21 days post-vaccination. Data was collected at 30 days post-challenge.

Table 1. Cumulative percent mortality (CPM), standard error (SE) of mortality and relative percent survival (RPS).

	CPM	SE	RPS
Negative Control	32	6.7	
killed IPNV 1x10^8 PFU/ml	9.9	1.3	69
pET30-VP2	14	2	56
pET30-gVP2	8.5	4	73
pET30-Hsp-VP2	6.7	2.3	79
pET30-polyprotein	16	0.6	50

Figure 1: Cumulative percent mortality (CPM) of rainbow trout fry vaccinated at 0.336 g and challenged with IPNV 3 weeks later at 0.49 g.

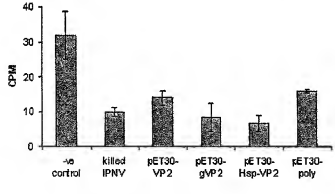


Figure 2: Relative percent survival (RPS) of vaccinated rainbow tout fry challenged with IPNV at a mean weight of 0.49 g.

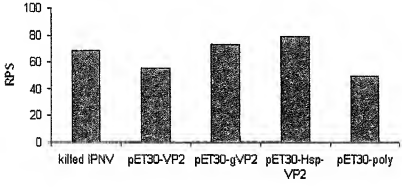
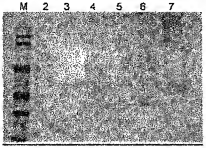


Figure 3: Western blot of recombinant IPNV vaccines loaded at 20 ug protein/well.

1. Marker
2. Pure IPNV
3. control BL21 cells
4. pET30-VP2
5. pET30-HSPVP2
6. pET30-gVP2
7. pET30poly



Trial 2

Fish were vaccinated with IPNV at a body weight of 0.195 g with the vaccine diluted to a fixed total protein content of 1.98 mg/ml. Fish were vaccinated by 1 minute immersion. Triplicate groups of 55 fish were challenged with IPNV at 25 days post-vaccination. Data was collected at 30 days post-challenge.

Figure 4: Cumulative percent mortality (CPM) of rainbow trout fry vaccinated at 0.195 g and challenged 25 days later with IPNV.

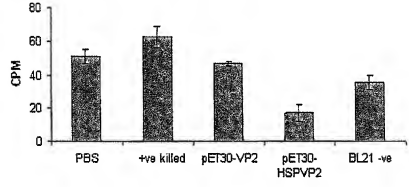


Figure 5: Relative percent survival (RPS) of vaccinated rainbow trout fry after IPNV challenge.